GANES CHEMICALS

GANES CHEMICALS INC.
630 BROAD STREET
CARLSTADT, NJ 07072
TELEPHONE: (201) 507-4300
TELEFAX: (201) 507-1930

March 30, 1999

1357 '99 MAR 31 A8:58

Mr. Kasturi Srinivasachar
Dockets Management Branch (HFA-305)
U.S. Food & Drug Administration
5630 Fischers Lane, Room 1061
Rockville, MD 20852

Dear Mr. Srinivasachar:

Let me begin by saying how much I enjoyed your presentation at the recent NAPM meeting in New York City. I thought the introduction to BACPAC II was helpful in determining my response to BACPAC I.

While I agree that BACPAC I is a big step in allowing post-approval changes, I still would like to make the case that you have placed the emphasis in the wrong location. As I stated during my presentation, DMFs are currently written by API manufacturers to such an extent as to allow changes inside the file process. This means that the customer initially doesn't have to know how the process is being run and therefore, can't determine when a change actually occurs. This is done by the API manufacturer to allow flexibility as he learns and operates the process at a commercial scale. Most processes are filed early in the learning curve, therefore, are not fully understood or developed. This occurs because of the need for speed to the market place, both from a commercial perspective and from a patient perspective.

I believe that the FDA should take a close look at who controls the process chemistry and make them the responsible party. While I recognize that review of DMFs could put additional work on the FDA's already taxed staff, I do believe the effort would not be a large increase if we could determine a mechanism for controlling the filing of DMFs. By this I mean, once a DMF is accessed by an applicant, then that DMF could in fact be reviewed and post changes to that DMF would automatically be considered for review. If a DMF was never accessed by an applicant, then that DMF would remain dormant. This should be a relatively simple process within the agency and controlled by how the numbers are applied to the DMF. Much like industry numbers its SOPs, once a DMF is accessed and initially approved, then its code number would indicate that any subsequent changes could be applied and reviewed as they occur. I believe for FDA and industry to get a true picture of post-approval changes, this needs to occur at the DMF level.

98D-0994

C20

In addition, I feel that the initial purpose of the DMF is to provide the API manufacturer with some security that his intellectual property will be protected. In the ever-growing Generic market, this becomes more and more important as economics is the overall driving force in this business segment. In order for both parties to be protected, i.e., the API manufacturer's intellectual property and the applicant's formulation, we need to determine a better way to review post-approval changes and ensure that both parties are protected. This review of the DMF in no way alleviates the API manufacturer's responsibility of notifying its customer when post-approval changes occur and ensuring that it does not affect his formulation. But in many cases, as products move into the Generic market, multiple customers with different needs and requirements, use common APIs and therefore, gaining post-approval changes by the customers becomes impossible. In many cases, some APIs have as many as 70 or more filed applications and as such, the API manufacturer can never secure an agreement between all of them that will be satisfactory. It's important to remember at this point that the API is a chemical entity that is clearly defined and well understood. It would be far better for the FDA to insist that all chemical and physical characteristics of an API be clearly defined as part of their acceptance criteria rather than try to have the applicant control post-approval changes in the API.

In summary, I believe all parties involved in the production, use, consumption and approval of APIs would be better served by placing the responsibility for post-approval changes on the DMF holder. Please consider the concept of DMF review in earnest before putting BACPAC in place.

Sincerely,

Christopher J. Smith
Director, Quality Assurance
& Regulatory Affairs

CJS/slf

FedEx USA Airbill

FedEx Tracking Number 808946111113

Form I.D. No. 0210

SPH32

Recipient's Copy

1 From

Date 3/30/99

Sender's Name Christopher J. Smith Phone (201) 507-4300

Company GANES CHEMICALS

Address 630 BROAD ST

Dept./Floor/Suite/Room

City CARLSTADT State NJ ZIP 07072

2 Your Internal Billing Reference Information

3 To

Recipient's Name Kasturi Srinivasachar Phone ( )

Company U.S. Food & Drug Administration
Dockets Management Branch (HFA-305)

Check here if residence (Extra charge applies for FedEx Express Saver)

Address 5630 Fischers Lane, Room 1061

(To "HOLD" at FedEx location, print FedEx address here) Dept./Floor/Suite/Room

City Rockville State MD ZIP 20852

For HOLD at FedEx Location check here

- Hold Weekday (Not available with FedEx First Overnight)
- Hold Saturday (Not available at all locations) (Available for FedEx Priority Overnight and FedEx 2Day only)

For WEEKEND Delivery check here (Extra Charge. Not available at all locations)

- Saturday Delivery (Available for FedEx Priority Overnight and FedEx 2Day only)
- NEW Sunday Delivery (Available for FedEx Priority Overnight only)

8 0 8 9 4 6 1 1 1 1 1 3

4a Express Package Service *Packages under 150 lbs.* Delivery commitment may be later in some areas.

- [X] FedEx Priority Overnight (Next business morning)
- [ ] FedEx Standard Overnight (Next business afternoon)
- [ ] FedEx First Overnight (Earliest next business morning delivery to select locations) (Higher rates apply)
- [ ] FedEx 2Day (Second business day)
- [ ] FedEx Express Saver (Third business day)

FedEx Letter Rate not available. Minimum charge: One pound rate.

4b Express Freight Service *Packages over 150 lbs.* Delivery commitment may be later in some areas.

- [ ] FedEx Overnight Freight (Next business day)
- [ ] FedEx 2Day Freight (Second business day)
- [ ] FedEx Express Saver Freight (Up to 3 business days)

(Call for delivery schedule. See back for detailed descriptions of freight services.)

5 Packaging

- [X] FedEx Letter (Declared value limit $500.)
- [ ] FedEx Pak
- [ ] FedEx Box
- [ ] FedEx Tube
- [ ] Other Pkg.

6 Special Handling (One box must be checked)

Does this shipment contain dangerous goods?*

- [X] No
- [ ] Yes (As per attached Shipper's Declaration)
- [ ] Yes (Shipper's Declaration not required)
- [ ] Dry Ice (Dry Ice, 9, UN 1845 ____ x ____ kg.)
- [ ] Cargo Aircraft Only

*Dangerous Goods cannot be shipped in FedEx packaging.

7 Payment

Bill to:

- [X] Sender (Account No. in Section 1 will be billed)
- [ ] Recipient
- [ ] Third Party
- [ ] Credit Card
- [ ] Cash/Check
- [ ] Obtain Recipient FedEx Account No.

(Enter FedEx Account No. or Credit Card No. below)

Total Packages	Total Weight	Total Declared Value*	Total Charges
[redacted]		$ .00	$

* When declaring a value higher than $100 per shipment, you pay an additional charge. See **SERVICE CONDITIONS, DECLARED VALUE, AND LIMIT OF LIABILITY** section for further information.

Credit Card Auth.

8 Release Signature

Your signature authorizes Federal Express to deliver this shipment without obtaining a signature and agrees to indemnify and hold harmless Federal Express from any resulting claims.

Questions?
Call 1·800·Go·FedEx® (800)463-3339

321

WCSL 0998
Rev. Date 7/98
Part #153023PS
©1994-98 FedEx
PRINTED IN U.S.A.

007331572 6